

**REMARKS**

Claims 1-46 were originally presented for examination.

In the first Office Action, mailed May 29, 2009, restriction was required between the following respective inventions:

Group I. claims 1-7 drawn to a first process comprising reacting a substrate with a biological catalyst in a hydrofluorocarbon in the presence of water.

Group II. claims 8-18 drawn to a second process comprising reacting a racemic mixture with a biological catalyst in a hydrofluorocarbon.

Group III. claims 19-29 drawn to a third process comprising reacting a meso compound to prepare a particular enantiomer with a biological catalyst in a hydrofluorocarbon.

Group IV. claims 30-46 drawn to a fourth process comprising reacting a prochiral compound with a biological catalyst in a hydrofluorocarbon.

Further, if Group I was elected, an additional species election of either protease or lipase from claim 4 was required.

In response to that first Office Action, applicants elected the Group I invention, claims 1-7, and the lipase species.

In the third and last Office Action, mailed April 15, 2010, the following final rejections were stated by the Examiner:

1. Claim 5 was rejected as indefinite under 35 U.S.C. §112 for stating "that the enzyme is part of a whole cell culture";
2. Claims 1-4 and 7 were rejected as obvious under 35 U.S.C. §103(a) over WO 98/42687 in view of the BEIER et al. publication;
3. Claim 6 was rejected as obvious under 35 U.S.C. §103(a) over WO 98/42687 in view of the BEIER et al. publication, and further in view of the JANDA et al. publication;

4. Claims 1-5 and 7 were rejected as obvious under 35 U.S.C. §103(a) over BLANCH et al. (4,925,790) in view of the FERRABOSCHI et al. publication; and
5. Claim 6 was rejected as obvious under 35 U.S.C. §103(a) over BLANCH et al. (4,925,790) in view of the FERRABOSCHI et al. and JANDA et al. publications.

Claim 5 was rejected under 35 U.S.C. §112 because as stated in the last Office Action the language “that the enzyme is part of a whole cell culture” is not clear whether applicants are attempting to claim that the enzyme is from a microbe or an animal. Claim 5 has been amended herein to set forth that the enzyme is part of a “microbial” whole cell culture. Basis for this amendment can be found, for example, on page 10, lines 4-18 and in the examples which use enzymes from microbial whole cell cultures. Accordingly, it is believed that with this amendment the §112 rejection of claim 5 has been overcome and should be withdrawn.

Claims 1-4 and 7 have been rejected as obvious over WO 98/42687 in view of the BEIER et al. publication, and claim 6 has been rejected as obvious over WO 98/42687 in view of the BEIER et al. publication, and further in view of the JANDA et al. publication.

Claim 1 sets forth a process which “is conducted in the presence of water at a level which is less than that required for the water to form a separate aqueous phase in the reaction system.”

In the last Office Action it is admitted that there is no mention in WO 98/42687 of the water content in the reaction disclosed therein.

Instead, the examiner relies on the BEIER et al. teaching that water is always present in a lipase reaction, as evidenced by the phrase “*essential water*” on page 1680, left-hand column, second paragraph of BEIER et al. However, this phrase must be put into the context of how the skilled person would read and understand BEIER et al. It is clear that BEIER et al. actually teaches that lipase reactions may be conducted in a dry medium. In particular, page 1680,

second paragraph teaches that "It is a remarkable feature of lipases that they retain their catalytic efficiency when suspended in **dry** hydrophobic solvents ...." (emphasis added)

Furthermore, at page 1681 in describing experimental condition BEIER et al. states "**dry** Na<sub>2</sub>SO<sub>4</sub> was added to **absorb** expelled water." (emphasis added).

The reference to "*essential water*" in BEIER et al. is with respect to water that is bound to the enzyme and associated with the maintenance of the secondary structure and of the conformation and mobility of the active site of the enzyme. Although the amount of "*essential water*" required varies according to the family of enzymes, it is usually a minimally-low amount; lipases are reported to require only a few molecules of water associated with each protein while Subtilisin and Chymotrypsin are reported to require around 50 molecules of water per protein. So while these systems do contain water, it is arguably at a level which would be regarded as *de minimis* by the skilled person; i.e. how much water does any "dry" system contain?

By use of "dry" solvents, clearly BEIER et al. is distinguishing between the water present in the bulk medium and that present as "*essential water*" in the enzyme. Further, BEIER et al. clearly teaches that solvents that are more polar than hexane would be expected to adversely affect the performance of the enzyme by stripping the "*essential water*" from the enzyme. This would teach away from the use of (hydro)fluorocarbons, all of which are more polar than hexane.

If (hydro)fluorocarbons were somehow to be contemplated, arguably in light of BEIER et al. they would be used at a solvent water content of at least saturation in order to avoid stripping of "*essential water*" as illustrated in the Advanced Photonics Limited patent (WO 99/13098) which is among the prior art cited by applicants upon the filing of the present application.

Therefore, there is clearly a difference between the reference to water in the present claimed invention as compared to the teaching of BEIER, et al.

Claims 1-5 and 7 have been rejected as obvious over BLANCH et al. in view of FERRABOSCHI et al., and claim 6 has been rejected as obvious over BLANCH et al. in view of FERRABOSCHI et al., and further in view of the JANDA et al. publication.

BLANCH et al. teaches in column 2, lines 58 to 61 that the supercritical fluids to be used according to their invention in the described reaction are carbon dioxide, oxygen, nitrous oxide, ethane, ethylene and trifluoromethane. The only one of those fluids which is a (hydro)fluorocarbon is the trifluoromethane. Claim 1 has been amended to expressly exclude trifluoromethane as one of the (hydro)fluorocarbon solvents used in the process claimed in Claim 1. There is no further teaching or suggestion of any other (hydro)fluorocarbons to be used in this type of enzyme-catalyzed reaction in either BLANCH et al., FERRABOSCHI et al. or JANDA et al.

Such exclusionary negative limitation is quite acceptable. As provided in MPEP §2173.05(i),

Any negative limitation or exclusionary provision must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining.") See also, *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984).

The requisite basis for the exclusion of trifluoromethane appears in the original specification at page 5, lines 22-23.

Furthermore, BLANCH et al. specifically teaches that the preferred supercritical fluid to be used is carbon dioxide because it has been found not to denature most enzymes (see, for example, column 3, lines 16 to 20 of BLANCH et al.).

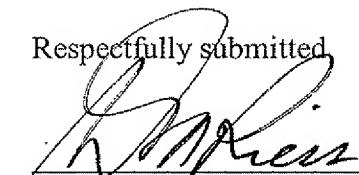
In summary, BEIER et al. fails to disclose or suggest a process which is conducted in the presence of water, and instead teaches the person skilled in the art to use dry solvents.

Neither FERRABOSCHI et al. nor JANDA et al. provides any motivation to use a (hydro)fluorocarbon solvent in an enzymatic reaction, and BLANCH et al. provides motivation for using only trifluoromethane in a supercritical state, but that preferably carbon dioxide should be used. There is no further teaching or suggestion in BLANCH et al. of any other (hydro)fluorocarbons to be used in the claimed enzymatic reaction other than the now expressly excluded trifluoromethane .

For the above reasons, it is respectfully submitted that all of the remaining elected claims in the present application, claims 1-7, are in condition for allowance. Accordingly, it is requested that the rejection of the claims be reconsidered and withdrawn, and that the application be allowed.

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